

SEQUENCE LISTING

<110> Amgen Inc.

<120> Crystal of a Kinase-Ligand Complex and Methods of Use

<130> A-747A

<140> US 09/574,559

<141> 2000-05-19

<150> US 09/574,630

<151> 2000-05-19

<150> US 60/134,965

<151> 1999-05-19

<160> 11

<170> PatentIn version 3.1

<210> 1

<211> 508

<212> PRT

<213> Homo sapiens

<400> 1

Gly Cys Gly Cys Ser Ser His Pro Glu Asp Asp Trp Met Glu Asn Ile
1 5 10 15

Asp Val Cys Glu Asn Cys His Tyr Pro Ile Val Pro Leu Asp Gly Lys
20 25 30

Gly Thr Leu Leu Ile Arg Asn Gly Ser Glu Val Arg Asp Pro Leu Val
35 40 45

Thr Tyr Glu Gly Ser Asn Pro Pro Ala Ser Pro Leu Gln Asp Asn Leu
50 55 60

Val Ile Ala Leu His Ser Tyr Glu Pro Ser His Asp Gly Asp Leu Gly
65 70 75 80

Phe Glu Lys Gly Glu Gln Leu Arg Ile Leu Glu Gln Ser Gly Glu Trp
85 90 95

Trp Lys Ala Gln Ser Leu Thr Thr Gly Gln Glu Gly Phe Ile Pro Phe
100 105 110

Asn Phe Val Ala Lys Ala Asn Ser Leu Glu Pro Glu Pro Trp Phe Phe
115 120 125

Lys Asn Leu Ser Arg Lys Asp Ala Glu Arg Gln Leu Leu Ala Pro Gly
130 135 140

Asn Thr His Gly Ser Phe Leu Ile Arg Glu Ser Glu Ser Thr Ala Gly
145 150 155 160

Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Gln Asn Gln Gly Glu Val
165 170 175

Val Lys His Tyr Lys Ile Arg Asn Leu Asp Asn Gly Gly Phe Tyr Ile
180 185 190

Ser Pro Arg Ile Thr Phe Pro Gly Leu His Glu Leu Val Arg His Tyr
195 200 205

Thr Asn Ala Ser Asp Gly Leu Cys Thr Arg Leu Ser Arg Pro Cys Gln
210 215 220

Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val Pro
225 230 235 240

Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe Gly
245 250 255

Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val Lys
260 265 270

Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu Ala
275 280 285

Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr Ala
290 295 300

Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu Asn
305 310 315 320

Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu Thr
325 330 335

Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met Ala
340 345 350

Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala Asn
355 360 365

Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly Leu
370 375 380

Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys
385 390 395 400

Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr Phe
405 410 415

Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu Ile
420 425 430

Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu Val
435 440 445

Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn Cys
450 455 460

Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg Pro
465 470 475 480

Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp Phe
485 490 495

Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro
500 505

<210> 2

<211> 285

<212> PRT

<213> Recombinant baculovirus

<400> 2

Gln Thr Gln Lys Pro Gln Lys Pro Trp Trp Glu Asp Glu Trp Glu Val
 1 5 10 15
 Pro Arg Glu Thr Leu Lys Leu Val Glu Arg Leu Gly Ala Gly Gln Phe
 20 25 30
 Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly His Thr Lys Val Ala Val
 35 40 45
 Lys Ser Leu Lys Gln Gly Ser Met Ser Pro Asp Ala Phe Leu Ala Glu
 50 55 60
 Ala Asn Leu Met Lys Gln Leu Gln His Gln Arg Leu Val Arg Leu Tyr
 65 70 75 80
 Ala Val Val Thr Gln Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met Glu
 85 90 95
 Asn Gly Ser Leu Val Asp Phe Leu Lys Thr Pro Ser Gly Ile Lys Leu
 100 105 110
 Thr Ile Asn Lys Leu Leu Asp Met Ala Ala Gln Ile Ala Glu Gly Met
 115 120 125
 Ala Phe Ile Glu Glu Arg Asn Tyr Ile His Arg Asp Leu Arg Ala Ala
 130 135 140
 Asn Ile Leu Val Ser Asp Thr Leu Ser Cys Lys Ile Ala Asp Phe Gly
 145 150 155 160
 Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala
 165 170 175
 Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn Tyr Gly Thr
 180 185 190
 Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Thr Glu
 195 200 205
 Ile Val Thr His Gly Arg Ile Pro Tyr Pro Gly Met Thr Asn Pro Glu
 210 215 220
 Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg Met Val Arg Pro Asp Asn
 225 230 235 240
 Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg Leu Cys Trp Lys Glu Arg
 245 250 255

Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu Arg Ser Val Leu Glu Asp
 260 265 270

Phe Phe Thr Ala Thr Glu Gly Gln Tyr Gln Pro Gln Pro
 275 280 285

<210> 3.

<211> 301

<212> PRT

<213> Artificial sequence

<220>

<223> See Figure 5 - ZAP70

<400> 3

Tyr Ser Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg
 1 5 10 15

Asp Asn Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly
 20 25 30

Ser Val Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val
 35 40 45

Ala Ile Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu
 50 55 60

Met Met Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile
 65 70 75 80

Val Arg Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met
 85 90 95

Glu Met Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg
 100 105 110

Glu Glu Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser
 115 120 125

Met Gly Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu
 130 135 140

Ala Ala Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser
 145 150 155 160

Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu Lys Val Lys
35 40 45

Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala
50 55 60

Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser Val Asp Asn
65 70 75 80

Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln
85 90 95

Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp Tyr Val Arg
100 105 110

Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn Trp Cys Val
115 120 125

Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg Leu Val His
130 135 140

Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro Gln His Val
145 150 155 160

Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala Glu Glu Lys
165 170 175

Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu
180 185 190

Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser
195 200 205

Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser Lys Pro Tyr
210 215 220

Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu Lys Gly Glu
225 230 235 240

Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met
245 250 255

Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Arg Glu
260 265 270

Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln Arg Tyr Leu
275 280 285

Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
290 295 300

Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
 305 310 315 320

Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser Pro
 325 330 335

Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser
 340 345

<210> 5

<211> 298

<212> PRT

<213> Artificial sequence

<220>

<223> See Figure 5 - CDK2

<400> 5

Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
 1 5 10 15

Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
 20 25 30

Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
 35 40 45

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
 50 55 60

Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
 65 70 75 80

Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
 85 90 95

Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
 100 105 110

Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
 115 120 125

Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
 130 135 140

Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
145 150 155 160

His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
165 170 175

Cys Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
180 185 190

Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
195 200 205

Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
210 215 220

Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
225 230 235 240

Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
245 250 255

Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
260 265 270

Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
275 280 285

Val Thr Lys Pro Val Pro His Leu Arg Leu
290 295

<210> 6

<211> 329

<212> PRT

<213> Artificial sequence

<220>

<223> See Figure 5 - PKA

<400> 6

Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu Ser Pro Ala Gln Asn Thr
1 5 10 15

Ala His Leu Asp Gln Phe Glu Arg Ile Lys Thr Leu Gly Thr Gly Ser
20 25 30

Phe Gly Arg Val Met Leu Val Lys His Lys Glu Thr Gly Asn His Tyr
 35 40 45

Ala Met Lys Ile Leu Asp Lys Gln Lys Val Val Lys Leu Lys Gln Ile
 50 55 60

Glu His Thr Leu Asn Glu Lys Arg Ile Leu Gln Ala Val Asn Phe Pro
 65 70 75 80

Phe Leu Val Lys Leu Glu Phe Ser Phe Lys Asp Asn Ser Asn Leu Tyr
 85 90 95

Met Val Met Glu Tyr Val Pro Gly Gly Glu Met Phe Ser His Leu Arg
 100 105 110

Arg Ile Gly Arg Phe Ser Glu Pro His Ala Arg Phe Tyr Ala Ala Gln
 115 120 125

Ile Val Leu Thr Phe Glu Tyr Leu His Ser Leu Asp Leu Ile Tyr Arg
 130 135 140

Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp Gln Gln Gly Tyr Ile Gln
 145 150 155 160

Val Thr Asp Phe Gly Phe Ala Lys Arg Val Lys Gly Arg Thr Trp Thr
 165 170 175

Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro Glu Ile Ile Leu Ser Lys
 180 185 190

Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala Leu Gly Val Leu Ile Tyr
 195 200 205

Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe Ala Asp Gln Pro Ile Gln
 210 215 220

Ile Tyr Glu Lys Ile Val Ser Gly Lys Val Arg Phe Pro Ser His Phe
 225 230 235 240

Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn Leu Leu Gln Val Asp Leu
 245 250 255

Thr Lys Arg Phe Gly Asn Leu Lys Asn Gly Val Asn Asp Ile Lys Asn
 260 265 270

His Lys Trp Phe Ala Thr Thr Asp Trp Ile Ala Ile Tyr Gln Arg Lys
 275 280 285

Val Glu Ala Pro Phe Ile Pro Lys Phe Lys Gly Pro Gly Asp Thr Ser
 290 295 300

Asn Phe Asp Asp Tyr Glu Glu Glu Ile Arg Val Ser Ile Asn Glu
 305 310 315 320

Lys Cys Gly Lys Glu Phe Ser Glu Phe
 325

<210> 7

<211> 275

<212> PRT

<213> Recombinant baculovirus

<400> 7

Met Asp Glu Trp Glu Val Pro Arg Glu Thr Leu Lys Leu Val Glu Arg
 1 5 10 15

Leu Gly Ala Gly Gln Phe Gly Glu Val Trp Met Gly Tyr Tyr Asn Gly
 20 25 30

His Thr Lys Val Ala Val Lys Ser Leu Lys Gln Gly Ser Met Ser Pro
 35 40 45

Asp Ala Phe Leu Ala Glu Ala Asn Leu Met Lys Gln Leu Gln His Gln
 50 55 60

Arg Leu Val Arg Leu Tyr Ala Val Val Thr Gln Glu Pro Ile Tyr Ile
 65 70 75 80

Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Val Asp Phe Leu Lys Thr
 85 90 95

Pro Ser Gly Ile Lys Leu Thr Ile Asn Lys Leu Leu Asp Met Ala Ala
 100 105 110

Gln Ile Ala Glu Gly Met Ala Phe Ile Glu Glu Arg Asn Tyr Ile His
 115 120 125

Arg Asp Leu Arg Ala Ala Asn Ile Leu Val Ser Asp Thr Leu Ser Cys
 130 135 140

Lys Ile Ala Asp Phe Gly Leu Ala Arg Leu Ile Glu Asp Asn Glu Tyr
 145 150 155 160

Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu
 165 170 175

Ala Ile Asn Tyr Gly Thr Phe Thr Ile Lys Ser Asp Val Trp Ser Phe
 180 185 190

Gly Ile Leu Leu Thr Glu Ile Val Thr His Gly Arg Ile Pro Tyr Pro
 195 200 205

Gly Met Thr Asn Pro Glu Val Ile Gln Asn Leu Glu Arg Gly Tyr Arg
 210 215 220

Met Val Arg Pro Asp Asn Cys Pro Glu Glu Leu Tyr Gln Leu Met Arg
 225 230 235 240

Leu Cys Trp Lys Glu Arg Pro Glu Asp Arg Pro Thr Phe Asp Tyr Leu
 245 250 255

Arg Ser Val Leu Glu Asp Phe Phe Thr Ala Thr Glu Arg His His His
 260 265 270

His His His
 275

<210> 8

<211> 39

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 8

cagaagagat ctatggagga cgagtgggag gttcccagg
 39

<210> 9

<211> 58

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 9

ccacaggaat tcagtgatgg tggatgatgat gacgtgtggc cgtgaagaag tcctccag
58

<210> 10

<211> 18

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer for baculovirus - See Example 8

<400> 10

gttctagtgg ttggctac
18

<210> 11

<211> 23

<212> DNA

<213> Artificial sequence

<220>

<223> DNA primer of baculovirus - See Example 8

<400> 11

cctctacaaa tgtggtatgg ctg
23